1 Gut cancer increases the risk for *Drosophila* to be preyed upon by hunting spiders

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23 Abstract

24 Predators are thought to prey on individuals that are in poor physical condition, although the evidence
 25 supporting this is ambiguous. We tested if sick individuals where more predated using *Drosophila*
 26 *melanogaster* flies as manipulable preys. We asked whether hunting spiders, trapped from the wild,
 27 would selectively prey upon flies with compromised health (i.e. chronically infected or cancerous)
 28 versus healthy flies under laboratory conditions. Flies chronically infected with the bacterium
 29 *Providencia rettgeri*, a natural *Drosophila* pathogen, were not selectively preyed upon by jumping
 30 spiders. We strengthened and confirmed our finding with another hunting spider species, small wolf
 31 spiders. We discuss that this result supports the hypothesis that chronic infection is associated with
 32 reduced symptoms notably to avoid the potentially deadly consequences of host predation on
 33 pathogens. We then induced colon cancer in some of the flies and asked whether the presence of
 34 cancer led to selective predation; there is little evidence for this, even in vertebrates. As the cancer
 35 developed, the incidence of predation by jumping spiders on the afflicted flies increased. We conclude
 36 that disease can have different lethal consequences through predation, even in invertebrate species, and
 37 that cancer is a factor in selective predation. Our results may explain why early tumours, but not
 38 metastasized cancers, are commonly detected in organisms in the wild, as cancer bearing individuals
 39 are rapidly eliminated due to the strong selective pressure against them.

40 Introduction

41 In vertebrates, individuals that are injured, or diseased are often preyed upon, as are juveniles who
 42 have not reached adult speed or reflex (Furey et al., 2021; Genovart et al., 2010; Mesa, Poe,
 43 Gadomski, & Petersen, 1994; Møller, 2008; Murray, 2002). This is especially true when a predator's
 44 preferred type of prey is difficult to catch at the prime of its performance (Temple, 1987), however,
 45 there are exceptions (Penteriani et al., 2008). Although this conventional wisdom of selective
 46 predation on substandard individuals is largely accepted, only a few studies have tested it empirically.
 47 Selective predation can only be said to exist when the relative frequencies of the types of prey in a
 48 predator's diet differ from the frequencies of the prey in the environment (Chesson, 1978). Hence, to
 49 test the selective prey hypothesis in the wild, data on the types of prey sought by many of the predators
 50 and the health status of the whole prey population would be determined. This is obviously difficult to
 51 obtain. Furthermore, a prey individual may suffer from different conditions which influence each other
 52 and lead to spurious effects. For example, exhaustion from care for large brood increases susceptibility
 53 to parasites (Oppliger, Christe, & Richner, 1996). Thus, the fittest hosts are the ones classified as
 54 being sick. Although those information may be vitally important in the context of eco-evolutionary
 55 dynamics (Brunner, Anaya-Rojas, Matthews, & Eizaguirre, 2017; Brunner, Deere, Egas, Eizaguirre, &
 56 Raeymaekers, 2019), the topic has been subjected more to speculation than to empirical study.

57 Probably the most studied question regarding selective predation is whether predators prey
 58 more on individuals with suboptimal conditions over healthy individuals. Even if hosts predators may
 59 avoid infected prey to avoid the risk of getting sick themselves (Goren & Ben-Ami, 2017), it has been
 60 suggested, based on field observations, that infections could increase the vulnerability to predation
 61 (Adelman, Mayer, & Hawley, 2017; Duffy, Hall, Tessier, & Huebner, 2005; Gooding et al., 2020;
 62 Miller et al., 2008; Moller & Erritzoe, 2000; Moller, Erritzoe, & Tottrup, 2010; Møller & Nielsen,
 63 2007; Murray, Cary, & Keith, 2006) and there is some experimental support for this (DeBlieux &
 64 Hoverman, 2019; Gallagher et al., 2019; Johnson, Stanton, Preu, Forshay, & Carpenter, 2006; Murray,
 65 2002). Consequently, by mediating selective predation, parasites can mediate the relationship between
 66 hosts and their prey (Hall, Cáceres, Duffy, & Cáceres, 2005; Møller, 2008). For instance, removing

67 predators can reduce vertebrate prey populations (Sih, Crowley, Mcpeek, Petranka, & Strohmeier,
68 1985), which seems counterintuitive, as predators are expected to remove preys. However,
69 mathematical models predict that virulent parasites may be selected against if predation
70 disproportionately removes them before they can be transmitted to the host (Packer, Holt, Hudson,
71 Lafferty, & Dobson, 2003). Without this check on virulent parasites by the predator, more prey may
72 die from lethal infections than from predation. Hence, if selective predation for infected individuals is
73 a common pattern, it may also be a major driver of host and parasite evolution and cannot be ignored
74 any longer (Møller, 2008).

75 It is also relevant to consider that not all sickness come from infections and that non-infectious
76 diseases could also increase the risk of being predated. In fact, understanding the role of cancer on
77 ecosystem function has been identified as a key endeavour (Dujon, Aktipis, et al., 2021). So far, most
78 of our knowledge is based on the consequence of transmissible cancer on an apex predator (i.e.
79 Tasmanian devil (Cunningham, Johnson, & Jones, 2020; Hollings, Jones, Mooney, & McCallum,
80 2014; Hollings, Jones, Mooney, & McCallum, 2016; Woods et al., 2018)), and few to nothing is
81 known about the potential selective predation of prey that are sick due to a non-infectious disease (see
82 (Perret, Gidoin, Ujvari, Thomas, & Roche, 2020) for a theoretical study). Mutations can occur during
83 the cell replication and division required to grow and maintain multicellular animals, and certain types
84 of mutation, said oncogenic mutations, can lead to the formation of tumours (Aktipis et al., 2015;
85 Albuquerque, Drummond do Val, Doherty, & de Magalhães, 2018; Hanahan & Weinberg, 2011;
86 National Cancer Institute, 2020a). In most cases, tumours are benign (Bissell & Hines, 2011), but they
87 can be malignant, and even fatal (Aktipis et al., 2015; Albuquerque et al., 2018; Hanahan & Weinberg,
88 2011; National Cancer Institute, 2020b). Clinical categorization of tumours has been established in
89 unchallenging, even ‘optimal’ environments (i.e. in the laboratory or clinic), usually to the point of
90 death via organ failure. The impact of tumour progression is likely to influence tremendously
91 individual’s life history traits (e.g. lifespan and reproductive output but also competitive and dispersal
92 ability, and pathogen susceptibility), yet, its impact under more natural conditions has largely been
93 neglected (Roche, Møller, DeGregori, & Thomas, 2017; Marion Vittecoq et al., 2013). Furthermore,

94 depending on the relationship between tumour development and the health of the prey, predation could
95 affect the selection of oncogenic mutations and thus the risk to develop cancer. To our knowledge, the
96 possible interactions between a predator and a prey that is afflicted with cancer are poorly understood
97 and have not been empirically studied to date (Marion Vittecoq et al., 2013).

98 Here, we induced chronic bacterial infection and colon cancer in prey to understand their role
99 in increasing the likelihood of being predated. We use the fruit fly *Drosophila melanogaster*, a model
100 which has started recently to be used to study the effect of cancer from an ecological perspective
101 (Arnal et al., 2017; Dawson et al., 2018) and is already a well-characterized model for infectious and
102 non-infectious diseases, as a novel model for sick prey. We assess the predation of flies by hunting
103 spiders, using flies chronically infected by a wild-caught bacterial pathogen (*Providencia rettgeri*),
104 and have genetically induced cancer, under laboratory-controlled conditions. These conditions allow
105 for the ideal experimental setting to study predation and the role of prey well-being in a population
106 context.

107 Materials and methods

108 Prey and predators.

109 We used *Drosophila melanogaster* flies as prey in this study as they are tractable to genetic induction
110 of tumours, are well-defined models for bacterial infection, and allow for control of environmental and
111 genetic differences. Only one sex (males) were used, to avoid sex effects. We induced chronic
112 infection by injecting 23 nL of a suspension of few thousand cells of the bacterium *Providencia*
113 *rettgeri* (strain *Dmel*, isolated from wild-caught *Drosophila melanogaster*; Juneja and Lazzaro 2009)
114 in phosphate-buffered saline (PBS) into the abdomen of flies (Canton S line, a wildtype genotype kept
115 in the laboratory since several decades). The same volume of sterile PBS without bacteria was injected
116 into another group of flies that served as the control. Individuals surviving for three days or more after
117 injection of the bacteria have an established chronic infection, as we have previously demonstrated
118 (Duneau et al., 2017).

To induce tumours in the flies, we took advantage of signalling pathways that regulate cell growth in mammals, which have a conserved function in *Drosophila*, the EGFR and Wnt pathways (Millburn et al., 2016; Mirzoyan et al., 2019; Rudrapatna, Cagan, & Das, 2012; Villegas, 2019). We used targeted induction of these pathways (Ras^{v12} for EGFR, APC RNAi for the Wnt pathway) to induce two types of enlargement of the flies digestive tract (i.e. hyperplasia, often called benign tumour, and cancer). Those types of colon cancer is appropriate for this study, as it does not overtly affect physical performance including locomotion, and will thus allow for the study of the interaction of oncogenic phenomena and predation (see Dawson et al. 2018 for locomotion assays in gut cancerous flies in another genetic background). To generate tumours in the gut of *Drosophila*, flies *esg^{TS}* (*esgGal4*, *Gal80^{ts}*, *UAS-GFP*) were crossed to either background control flies (Trip stock 35786), flies carrying a *UAS-Ras^{v12}* (Bloomington 64196) or flies carrying a combination of *UAS-Ras^{v12}* (Bloomington 641926) and *UAS-APC-RNAi* (Bloomington Trip stock 28582) combined. The expression of Ras^{v12} in progenitor cells stimulates an accelerated turnover and a mild accumulation of epithelial cells in the gut, akin to a dysplastic tissue (Buchon, Broderick, Kuraishi, & Lemaitre, 2010; Houtz, Bonfini, Bing, & Buchon, 2019), later also referred as hyperplasia. The overexpression of *Ras^{v12}* combined with the knock-down of *APC* leads to increased proliferation, and accumulation of progenitor cells and epithelial cells in the gut, reminiscent of an intestinal disseminated tumour (Wang et al., 2013), later also referred as cancerous. F1 flies from these crosses were raised at 18°C (*Gal4* off, transgene expression off, normal development and emergence), and 3 days after emergence were switched to 29°C (*Gal4* on, transgene expression on) for 10 or 20 days before performing the experiment. As in (Wang et al., 2013), crosses with WT flies showed mild tissue renewal (restricted GFP signal), flies with expressing *Ras^{v12}* showed disseminated GFP in their gut and flies expressing *Ras^{v12}* and *APC RNAi* showed gut enlargement and GFP accumulation. The longest the induction is done and the strong is the phenotypes leading to a gradient from induced hyperplasia for 10 days (i.e. mild colon enlargement) to induced cancer for 20 days (i.e. limit to the complete obstruction of the colon).

We used two families of hunting spiders as predators: jumping spiders of several species from the family of Salticidae (see illustration in Fig. 1) and small wolf spiders from the family of Lycosidae

(likely *Pardosa lugubris*). Both jumping and wolf spiders hunt by wandering rather than by using webs as traps.

Jumping spiders have the sharpest vision of any arthropod, even surpassing many vertebrates (Land & Nilsson, 2012). They hunt during the day and rely on this astonishing vision when catching a prey. Similar to the way a cat stalks its prey, jumping spiders turn towards their prey, directed by a pair of lateral eyes that provide a nearly panoramic field of view with the ability to discern motion (Zurek & Nelson, 2012). Then, the spiders track, approach, and jump on the prey. The vision accuracy is conferred by two pairs of forward-facing eyes that also provide a precise perception of depth (Nagata et al., 2012; Zurek, Taylor, Evans, & Nelson, 2010).

After having tested jumping spiders as predator, we decided to test whether infected individuals would still not be more likely to be eaten by another type of hunting spider species with different hunting behaviour, wolf spiders. This was additionally performed to strengthen our “negative” result. Wolf and jumping spiders have already successfully been used to test for selective predation (Holmberg & Turnbull, 1982; Vickers & Taylor, 2018). Wolf spiders are generally nocturnal hunters and their eyes function mainly as low-light movement detectors, however *Pardosa* species are mostly hunting during the day (Edgar, 1969). Their vision is not as acute as that of jumping spiders (Land & Nilsson, 2012). The use of visual cues in prey detection and orientation have only been well-studied in jumping spiders, and empirical evidence suggests that wolf spiders rely more on vibrations to capture their prey than on vision (Lizotte & Rovner, 1988). Hence, the differences between these two types of hunting spiders primarily lie in their ability to prey on flies that are at rest. In an environment where there is no place to hide, jumping spiders would likely prey equally well on moving and non-moving prey, and selective predation in this case should depend largely on the prey’s capacity to escape.

Predation trials

Predation trials were performed during the day by incubating five healthy and five sick flies, age-matched, at 20°C with a spider in a round plastic box (11.5cm x 8.5cm, see illustration in fig. 1B)

containing a wet piece of cotton or foam. The flies were first added to the box to settle before the introduction of the predators. After about 30 min, spiders were put in the box. The trials generally lasted for about 4 hours or were stopped when 50% of the flies had been preyed upon, as, when scoring only at the end of the experiment, it allows to score the most extreme result (i.e. all individuals from one treatment have been eaten before the other treatment). Even if no spiders were starved before the experiment, this goal was sometimes exceeded as some spiders ate faster than expected. Individual spiders have never been used twice as predators within an experiment.

To determine the number of surviving flies that were infected, we ground the remaining flies at the end of the predation period and suspended the mixture in 250 μ L of Luria-Bertani (LB) medium. A droplet of five microliters of the resulting suspension was spread on a petri dish filled with agar containing LB medium, and the plates were incubated overnight at 37°C to assess for the presence of *P. rettgeri*. We calculated the proportion of infected flies at the end of predation period by determining the number of droplets in which *P. rettgeri* were present. For a control comparison, we performed the same process with infected and healthy flies, but did not expose them to predatory spiders. Our protocol consistently led to the induction of tumour, even if interindividual variation in tumour size exist which can be a source of variation in our trials. In the unlikely event that some individuals were considered has carrying a tumour but did not, those individuals would reduce the strength of our signal as they would be like control individuals. The number of surviving flies that had cancer were counted by dissecting all surviving flies and observing their guts under a fluorescent microscope, which reveals the presence/absence of cancer.

Statistical analysis

Statistical analysis were performed using R, version 4.1 (R Core Team, 2020). The use of the Fisher exact test or a chi-squared test would have permitted us to test for every trial regardless of whether the number of flies from a particular category was more or less preyed upon than those from another category. However, we used a hypergeometric distribution instead of a Chi-squared distribution because, as flies were preyed upon, the population size decreased and we only had information on predation rate per treatment at the end of the experiment. The *p*-value for each experimental trial was

added up and compared to the summed p -value obtained by simulating random trials. We assessed the overall p -value by determining the number of simulated trials required to have an observed result (summed p -value observed) as probable as the simulation (summed p -value simulated). Hence, a p -value of 0.05 indicated that 20 trials would be sufficient to have the same result as the empirical data by chance, whereas a p -value of 0.0001 meant that 10,000 trials would be required to achieve the same result as the empirical data by chance. We used the Manly Alpha Index as the preference index to illustrate the selective predation on sick individuals (index 0: preference for healthy individuals, index 0.5: no preference, index 1: preference for sick individuals). It was calculated as $\log(\text{total flies sick} / \text{flies sick but not eaten}) / [(\log(\text{total flies sick} / \text{flies sick but not eaten}) + \log(\text{total flies healthy} / \text{flies healthy but not eaten}))]$ as established by Manly (1972). To test whether the preference index for sick individuals increased with the severity of the cancer, we considered hyperplasia after 10 and 20 days of induction and cancer after 10 days and 20 days as ordinal variables. This was used because although we knew the rank of severity (i.e. from inducing hyperplasia for 10 days to inducing cancer for 20 days), we could not know the size of the differences among them. This allowed us to test in a single model (i.e. using an ordinal logistic regression) for the increase of the preference index with the increase in cancer severity.

Ethical note

All spiders in the study were obtained from the wild during their daily activity and kept for less than a week, eventually fed with healthy *Drosophila*. Spiders used for testing the effect of cancer were sampled and tested on the Cornell University campus (Ithaca, NY, USA) and those used for testing the effect of infectious diseases were sampled and tested on the campus of the University of Toulouse 3 (Toulouse, France). All individuals have been released in the wild at the area they have been caught shortly after the experiments were performed.

Results

Predation of chronically infected flies by hunting spiders. We tested whether chronic infection of the male flies by *P. rettgeri* affected the risk of being preyed upon by the spiders. The flies had been infected for several days before exposure to the spiders, and their immune response was expected to be activated (Chambers, Jacobson, Khalil, & Lazzaro, 2019). Despite using two predator species, we did not detect selective predation by either of the hunting spider types (Fig. 2A and B for jumping and wolf spiders, respectively).

Predation of flies with cancer by hunting spiders. We asked if cancer of the gut, which we induced, affected the risk for predation of male flies by the hunting spiders. Hyperplasia is the enlargement of an organ or tissue caused by increased cell division and is often an initial stage in the development of cancer. We observed that flies in this early hyperplastic stage ($esg^{ts} > UAS-Ras^{v12}$) did not show an increased likelihood of getting preyed upon by the jumping spiders, which are active diurnal hunters (Fig. 3A). However, jumping spiders did catch more successfully flies with an advanced stage of cancer ($esg^{ts} > UAS-Ras^{v12}, UAS-APC-IR$) compared with healthy flies. Furthermore, the preference index for sick individuals increased with the length of time after the tumour had been induced (Fig. 3B).

Discussion

Many diseases do not kill their hosts and are considered benign in optimal conditions, such as in a clinic or laboratory. However, it is very likely that non-lethal illnesses still increase the risk of mortality through indirect interactions with other environmental factors. Indeed, being sick may reduce foraging and mating abilities, increase the risk for lethal superinfections, or of being preyed upon. Even though many biological questions are presently being addressed using an integrative approach, the question of whether a non-lethal disease is truly benign in natural conditions seems to have been overlooked in many cases. We hope to generate interest in evaluating the lethality of diseases when their interaction with other risks, such as predation, is considered. Chronic infection by

a wild-caught *Drosophila* pathogen did not significantly affect the risk of being preyed upon in the laboratory. In contrast, we observed that while the presence of early stage tumours did not change predation risk, the presence of advanced cancer did compared to age-matched controls.

Little is known about selective predation in individuals with non-infectious diseases. The prevailing opinion that general health, which can be affected by non-infectious sickness, correlates with the risk of being preyed upon, is largely observational (Genovart et al., 2010; Hoey & McCormick, 2004). Nonetheless, although we should not be jumping to hasty conclusions, our results on the effects of non-infectious disease on selective predation suggests a stronger selective pressure than natural chronic infections.

Cancers are common in multicellular organisms and can occur whenever cells evade the normal cell checkpoints that control cell division, proliferation, and apoptosis, thus leading to uncontrolled cell division (Aktipis et al., 2015). Individuals always have some tumours, most of which never become lethal (Abu-Helil & van der Weyden, 2019; Bissell & Hines, 2011). Our understanding of oncogenic phenomena in wild populations of animals is limited, in particular whether tumours that are clinically non-lethal affect the well-being of organisms in the wild (McAloose & Newton, 2009; Pesavento, Agnew, Keel, & Woolard, 2018; M. Vittecoq et al., 2015; Marion Vittecoq et al., 2013). Theoretical modelling further suggests that biotic interactions complicate the predictions regarding the impact of cancer on populations and that prey and predator populations are likely to suffer differently (Perret et al., 2020). If tumour formation is inevitable, it is likely that multicellular organisms have evolved ways to control and tolerate them, perhaps resulting in a trade-off between surviving the tumour and surviving other perils, such as infections or predation (Pavard & Metcalf, 2019). In some cases, selection for tumour tolerance may have arisen from selection for tolerance to other factors, perhaps explaining why early stages of cancer, such as the colon hyperplasia that we induced in *Drosophila*, do not change the likelihood of being preyed upon. In our study, when the tumour developed into a cancer, predation of the flies increased, suggesting that uncontrolled tumours strongly increase the likelihood of being preyed upon. This conclusion supports the idea that individuals with uncontrolled tumours will suffer the risk of increased predation compared with healthy individuals.

Predation is a critical force shaping natural selection (Wade & Kalisz, 1990). By removing prey genotypes susceptible to tumours, predators are likely to have selected for the tumour tolerance largely observed in nature (Bissell & Hines, 2011). Furthermore, by removing individuals with advanced tumours, predation may explain why cancerous animals are rarely recorded in autopsies of wild animal populations (Marion Vittecoq et al., 2013).

We do not know why cancerous flies are more predated than their age-matched controls or even if this result could be to some extent dependent on the sex of the fly. Jumping spiders have been shown to be able to choose prey based on odour and coloration (Vickers & Taylor, 2018). It would be difficult to interpret why such behaviour would have evolved in the context of cancer but we cannot exclude that, spiders recognized and preferred eating cancerous flies. Assays in gut cancerous flies from another study in another genetic background suggests that induction of colon cancer does not affect strongly fly locomotion (Dawson et al., 2018). However, there is still the possibility that cancerous flies have worst reflex than healthy flies or that subtle locomotion differences may be enough to explain a difference in the chance to escape predation. Our results lay the premise of future studies on understanding the mechanisms explaining the reasons for this difference.

The progression of cancer can, in many ways, be compared with infectious diseases. In fact, cancer cells have already been considered as a parasitic species consuming the host's resources after having emerged from healthy cells (Capp & Thomas, 2020; Duesberg, Mandrioli, McCormack, & Nicholson, 2011). However, if both reduce viability and survival, infectious diseases are, unlike oncogenic processes, under selective pressure to ensure transmission of the pathogen to another host. For both non-infectious diseases and cancer, selective predation could increase the selection against the sickness, as diseases that are moderate and non-lethal could lead to a higher risk of the host being preyed upon, resulting in mortality rates that are similar to those of infectious diseases. With infectious diseases, there may be additional consequences. First, selective predation could affect the transmission of pathogens, spreading them through predator feces over long distances. Second, it might affect epidemics, either preventing them by removing parasite spreaders from the host population (Duffy et al., 2005) or by increasing their likelihood of occurrence by dispersing parasites instead of containing

them in dead hosts (Strauss et al., 2016). An additional consideration is that predation may affect the evolution of parasite virulence. It is generally assumed that predation can reduce virulence because hosts with rapidly proliferating parasites would suffer more from the infection and may be eaten before transmitting the parasite to another host, whereas the less rapidly proliferating parasite would impact less host health and would be transmitted before the host is eaten (Moller et al., 2010). However, lower virulence could evolve also through lower pathogenicity, that is by inducing less damage to the host, and not only through reduced proliferation. The most important factor being that bacteria can proliferate within their host as long as the symptoms do not increase the risk of predation. The bacteria studied here, *P. rettgeri*, was obtained from the wild and is prevalent in populations of *D. melanogaster* (Juneja & Lazzaro, 2009). Despite being chronic and the fact that the pathogen can trigger an immune response through the course of the infection (Chambers et al., 2019; Duneau et al., 2017), the chronic infection did not increase the predation by the two species of predator we used in our study. This result supports the hypothesis that chronic infections are selected for such that the symptoms that enhance predation are reduced.

It is reasonable to assume that the success of predators is not simply due to favourable luck. In fact, selective predation may be more the rule than the exception and is likely to have a role on the evolution of diseases, infectious or not (Møller, 2008). On the one hand, selective predation on sick individuals is likely to counter-select against parasites or genetic diseases more strongly than if selection occurred upon disease-mediated host death later in life in absence of predation. On the other hand, in the same way that some parasites evolved to manipulate their host to increase transmission to intermediate hosts (Hughes & Libersat, 2019), parasites may have evolved to make their hosts less conspicuous to predation, for example, by interfering with the search for mates or by lessening the effects of the disease on the host; for example, by reducing symptoms. Because cancer progression generally results in the death of the organism, we cannot expect the incidence of lethal cancer to have evolved in the same way as parasites, except for transmissible cancers such as in Tasmanian devils (Dujon, Bramwell, Roche, Thomas, & Ujvari, 2021). We argue that selective predation on prey with

cancer may be one of the reasons why tumours are commonly tolerated in animals, where advanced cancer is only rarely detected.

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Figure legends

Figure 1. Photograph of a jumping spider consuming *Drosophila melanogaster* flies in the laboratory.

Figure 2. Predation by hunting spiders on a population of *Drosophila melanogaster* Canton S, of either healthy flies or flies chronically infected with *P. rettgeri*. A. Predation by jumping spiders (Hypergeometric test: $n = 27$ trials, p -value > 0.05 , Median pref. index = 0.64) B. Predation by wolf spiders (Hypergeometric test: $n = 30$ trials, p -value > 0.05 , Median pref. index = 0.43). Each dot represents the proportion of individuals eaten over five flies and the lines connect the groups of individuals from a same trial. Each trial represents ten flies (five from each type) presented to one spider at once. Preference index is calculated as in Manly (1972) and ranges from 0 to 1, from a preference to healthy flies to a preference for sick flies, respectively.

Figure 3. Predation by jumping spiders in a population of *Drosophila melanogaster* that were either healthy or in which colon tumours (hyperplasia) had been induced. Tumour size increased with induction time, during which uncontrolled cell division occurred. A. Uncontrolled cell division was triggered for 10 or 20 days in $esg^{TS} > Ras^{v12}$ flies to lead to hyperplasia (respectively with $n = 17$ and 15 trials). In both cases, individuals with hyperplasia were not differently predated upon compared with the healthy individuals. B. Fast uncontrolled cell division was triggered for 10 or 20 days in $esg^{TS} > Ras^{v12}$, *APC-RNAi* flies to lead to cancer (respectively with $n = 16$ and 20 trials). In both cases, individuals with cancer were more likely to be predated upon than individuals which did not have cancer. This pattern tended to be stronger as the tumour grew larger (Ordinal logistic regression: LRT=8.07, df=1, $p=0.004$). Each dot in A and B represents the proportion of individuals eaten over five flies and the lines connect the groups of individuals from a same trial. Each trial represents ten flies (five from each type) presented to one spider at once. Preference index is calculated as in Manly (1972) and ranges from 0 to 1, from a preference to healthy flies to a preference for sick flies, respectively.

A **B**